IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

ENDO PHARMACEUTICALS INC., Plaintiffs, v. ROXANE LABORATORIES, INC., Defendant.	C.A. No. 13-cv-3288-TPG

MEMORANDUM IN SUPPORT OF ROXANE LABORATORIES, INC.'S MOTION *IN LIMINE* REQUESTING THAT THIS COURT, ON COLLATERAL ESTOPPEL GROUNDS, PRECLUDE ENDO PHARMACEUTICALS INC. FROM TAKING POSITIONS INCONSISTENT WITH THE FEDERAL CIRCUIT IN *In re Kao*, 639 F.3d 1057 (Fed. Cir. 2011)

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CASES

Defendant Roxane Laboratories, Inc. moves *in limine* for the Court to apply the doctrine of collateral estoppel to bar Plaintiff Endo Pharmaceuticals Inc. from taking positions in this case that are inconsistent with the Federal Circuit's ruling in *In re Kao*, 639 F.3d 1057 (Fed. Cir. 2011), which concerned the same issues and subject matter at issue here and the same or related Endo patent applications that led to the patents-in-suit.

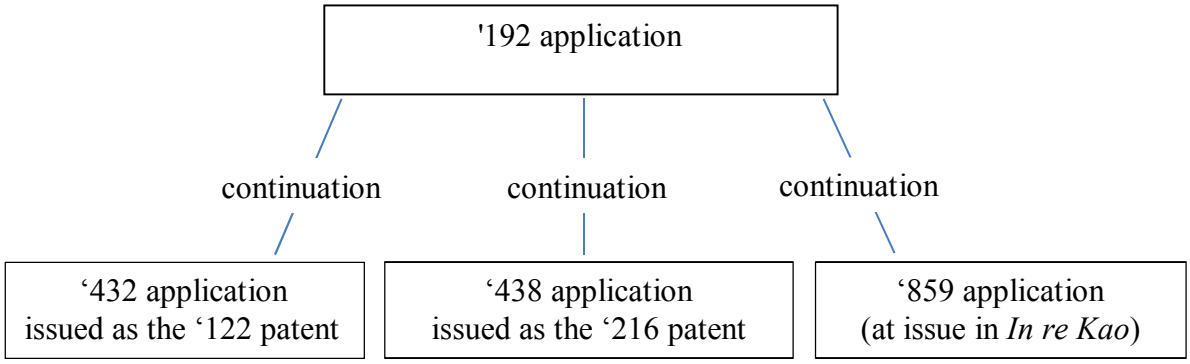
In *In re Kao*, the Federal Circuit considered Endo's appeal of a decision of the U.S. Patent and Trademark Office's Board of Patent Appeals and Interferences ("Board" or "BPAI") that itself upheld the patent office's determination that the pending claims of certain of Endo's patent applications were obvious, including one application which later issued as U.S. Patent No. 8,309,122 ("the '122 patent") at issue in this litigation. In its ruling, the Federal Circuit made numerous findings that apply to the '122 patent and to U.S. Patent No. 8,329,216 ("the '216 patent") in suit here. Those findings should not be relitigated here—under principles of collateral estoppel, Endo must be bound by them.

I. BACKGROUND

Underlying decisions

In re Kao reviewed decisions of the Board concerning three patent applications from a family of applications assigned to Endo. The Board had affirmed patent examiners' determinations that pending claims of these three U.S. Patent Applications (Nos. 11/680,432 ("the '432 Application," issued as the '122 patent), 12/167,859 ("the '859 Application"), and 11/766,740 ("the '740 Application")) were obvious in view of Patent Cooperation Treaty Publication No. WO 01/08661, a reference that we will call Maloney or WO '661. *See* Ex. 1, *In re Kao*, 639 F.3d at 1061-65; Ex. 2, Maloney.

The ‘432 application and the ‘859 application are directly related to the ‘122 and ‘216 patents in the current litigation. First, the ‘432 application issued as the ‘122 patent. *See* Ex. 3, ‘122 Patent at 1. And second, the ‘122 and ‘216 patents and the ‘859 application (now abandoned) are all direct descendants of U.S. Patent Application No. 10/190,192 (“the ‘192 application”) as follows:



See id.; Ex. 4, ‘216 Patent at 1; Ex. 5, ‘859 Application FH at July 11, 2008 Filing Receipt at 1. Because the ‘122 and ‘216 patents, as well as the ‘859 application, are continuations of the same ‘192 application, they all share the same patent specification. In addition, the ‘122 and ‘216 patents and the ‘859 application share highly similar claims covering the same subject matter—namely solid oral dosage forms (and methods of administering them to treat pain), comprising about 5 mg to about 80 mg oxymorphone in a controlled release delivery system comprising a hydrophilic material with a release rate profile designed to provide an adequate blood plasma level over at least 12 hours to provide sustained pain relief. *Compare* Ex. 3, ‘122 Patent at 25:50-28:5; Ex. 4, ‘216 Patent at 26:35-34:60; *with* Ex. 6, ‘859 Application FH at November 24, 2008 Amendment at 2-6. The claims of the ‘859 application also recite the same food effect limitation concerning a 50% increase in C_{max} in the fed state that is present in the claims of the ‘216 patent. *Id*.

The patent examiner reviewing the '432 and '859 applications had rejected all of the pending claims in the '432 and '859 applications as being obvious in view of Maloney. The patent examiner in rejecting the claims of the '432 application reasoned as follows:

> [Maloney] teaches oral sustained release preparations of opioid analgesics such as morphine, oxymorphone, etc (page 9, page 10, 2nd paragraph), wherein the active agents effecting [*sic*] for treating pain are embedded in a matrix of polymers (page 8) such as those described in the instant application. [Maloney] teaches that the amount of opioid analgesic ranges from 0.1-500 mg (page 11), for release up to 12 hours after administration. [Maloney] teaches preparing sustained release compositions of several opioid analgesics and in particular prefers oxycodone, oxymorphone etc (page 17, last lines of para 1).
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> * * *
>
> The example compositions of [Maloney] include methocel K100M, which is a hydrophilic polymer. Thus, the polymers of [Maloney] meet the instant claimed (claim 5) limitation that the material forms a gel upon exposure to gastrointestinal fluid.

Ex. 7, '122 Patent FH at April 28, 2008 Office Action at 5-6; *see also* Ex. 8, '859 Application FH at January 12, 2009 Office Action (examiner rejected the claims of the '859 patent providing similar reasoning).

Endo then, in an attempt to overcome the examiner's rejection of the claims of the '432 application, amended the claims, filed declarations, and presented attorney argument as to why Endo believed the pending claims were nonobvious. *See* Ex. 9, '122 Patent FH at May 28, 2008 Amendment and Response. But, the patent examiner was unpersuaded and maintained the obviousness rejections over Maloney. *See* Ex. 10, '122 Patent FH at August 6, 2008 Office Action; *see also* Ex. 8, '859 application FH at January 12, 2009 Office Action.

Endo appealed to the Board the examiner's rejections of the claims of the '432 and '859 application over the Maloney reference. The Board's decision on appeal affirmed the Examiner's obviousness rejection. *See* Ex. 11, '122 Patent FH at November 13, 2008 Appeal;

Ex. 12, January 12, 2010 Patent Board Decision; Ex. 13, '859 Application FH at March 2, 2009 Appeal; Ex. 14, January 12, 2010 Patent Board Decision.

Federal Circuit decision

Endo then appealed the January 2010 Board decisions to the Federal Circuit. *See* Ex. 15, '122 Patent FH at March 5, 2010 Notice of Appeal to the Federal Circuit; Ex. 16, '859 Application FH at March 5, 2010 Notice of Appeal to the Federal Circuit. The Federal Circuit's decision upheld the Board's decision that the claims of the '859 application were invalid and confirmed numerous findings of fact regarding the teachings of Maloney. As for the obviousness of the '432 application claims over Maloney, the Federal Circuit issued a judgment vacating and remanding the January 13, 2010 Board decision for consideration of whether (i) the record on appeal from the Board contained substantial evidence correlating the dissolution ranges in Maloney (based on the Basket Method) with the claimed ranges in Endo's pending claims (based on the Paddle Method)– *i.e.*, filling the proverbial "gap;" and (ii) "the importance, or lack thereof, of the claimed range to the alleged nonobviousness of the invention…." *In re Kao*, 639 F.3d at 1067. Those two issues concerned only the '432 application claims because the '859 application claims did not call for any dissolution requirements.

In analyzing obviousness of the claims of the '432 and '859 applications over Maloney, the Federal Circuit made or confirmed numerous findings concerning Maloney's teachings about extended-release oxymorphone compositions, the inherency of the pharmacokinetic and food-effect properties of oxymorphone when a person takes oxymorphone, and the enablement of Maloney. Specifically, the *Kao* court agreed with and accepted at least the following findings from the Patent Office:

1. "**it would be obvious to substitute oxymorphone in Maloney's Formula 6**[1]." *In re Kao*, 639 F.3d at 1066;

2. "**Maloney teaches a controlled release opioid formulation comprising an opioid compound in amounts of 5–100 mg**." *Id*. at 1071;

3. "**Maloney further discloses that oxymorphone is a preferred opioid compound**." *Id*.;

4. "Maloney discloses that its dosage form provides a dissolution rate of 60%–80% active agent released after 12 hours. Based on these findings, the Board reasonably concluded that **Maloney's active agent would still be effective after 12 hours** because it is still being released from Maloney's dosage form at 12 hours. . . . Substantial evidence supports the Board's conclusion that **the oxymorphone formulation disclosed in Maloney would satisfy the claimed 12–hour effectiveness limitation**." *Id*.;

5. "Substantial evidence supports the Board's finding that **Maloney teaches a controlled release formulation using both hydrophobic and hydrophilic materials**." *Id*.;

6. "It is **undisputed that Maloney discloses a method of providing extended pain relief by the provision of a therapeutically effective amount of controlled release oxymorphone**." *Id*. at 1072;

7. "**Maloney's express teachings render the claimed controlled release oxymorphone formulation obvious**, and the claimed "food effect" adds nothing of patentable consequence." *Id*. at 1070.

In addition, the court in *Kao* held as a matter of law that reciting inherent properties of oxymorphone cannot render patentable an otherwise obvious controlled-release oxymorphone composition. The court agreed with the Patent Office that the pharmacokinetic properties, including the food-effect properties and multiple peaks, were inherent to the oxymorphone compound itself:

1. As noted above, "Maloney's express teachings render the claimed controlled release oxymorphone formulation obvious, **and the claimed "food effect" adds nothing of patentable consequence**." *Id*.

2. "This court agrees with the Office. **Substantial evidence supports the Board's finding, based upon the specification, which confirms that the claimed "food effect" is an inherent property of oxymorphone itself, present both in**

[1] Emphasis added in bold to the *Kao* findings of fact.

> **controlled release and immediate release formulations of that drug.**" *Id*. at 1070;
>
> 3. "**The only evidence of record indicates that the unexpected in vivo characteristics [multiple peaks] of oxymorphone controlled release compositions did not result from properties unique to any specific commercial embodiment**." *Id*. at 1068-69.

Further, at the Federal Circuit, Endo argued that the Maloney reference was not enabled, but the Federal Circuit rejected the argument:

> The Office responds that the Board found that Maloney expressly teaches using oxymorphone in the disclosed formulations. Although Endo's experts essentially stated their view that Maloney did not enable the disclosed oxymorphone formulation, their statements were based on various "concerns" that fall short of establishing that the Maloney reference was nonenabling.

Id. at 1071.

The *Kao* court found that Maloney rendered the limitations in the pending claims regarding a controlled-release oxymorphone formulation obvious. The only remaining issue left after the *Kao* decision is whether the Basket Method dissolution test profile described in Maloney renders obvious the Paddle Method dissolution profiles claimed in the patents-in-suit – the "gap." Roxane has evidence to fill that gap and will show at trial that the asserted claims of the '122 and '216 patents are obvious.

II. ARGUMENT

Roxane brings this motion because this Court should not be forced to reconsider what Endo already argued against and lost before the Patent Examiner, the Board of Patent Appeals and Interferences, and the Federal Circuit.

"Under the doctrine of collateral estoppel, or issue preclusion, a final judgment on the merits in a prior proceeding precludes relitigation of those issues that were actually litigated and determined in the first suit, 'regardless of whether the two suits are based on the same cause of

action.'" *Medinol Ltd. v. Guidant Corp.*, 341 F. Supp. 2d 301, 313-314 (S.D.N.Y. 2004) (quoting *Postlewaite v. McGraw–Hill*, 333 F.3d 42, 48 (2d Cir. 2003)). Collateral estoppel doctrine promotes judicial efficiency and prevents inconsistent decisions. *Id*. at 314.

The party moving for institution of the doctrine of collateral estoppel must satisfy the following elements:

1. "the issues presented in the instant action are identical to those involved in the prior action;"
2. "the issues were actually litigated and decided in the prior action;"
3. "the estopped party had a full and fair opportunity to litigate the issues in the prior action;" and
4. "resolution of the issues was necessary to the final judgment."

Id. Endo bears the burden of showing that it did not have a full and fair opportunity to litigate the issues sought to be estopped. *Id*.

In addition, collateral estoppel may apply to legal claims that were not previously adjudicated because the "issues litigated, *not* the specific claims around which the issues were framed" are determinative. *Id*. (quoting *Westwood Chem., Inc. v. United States*, 525 F.2d 1367, 1372 (1975)). Thus, "application of collateral estoppel in the context of patent validity is premised on the identity of those issues that were previously litigated." *Id*.; *see also id.* at 321-324. For the reasons set forth below, Endo should be collaterally estopped from presenting argument that are inconsistent with the findings of the Federal Circuit decision. *See*, *e.g.*, *id*. at 321-323.

Are the issues presented in this action identical to those involved in the prior action?

Yes. Currently at issue in this case are assertions of invalidity of the patents-in-suit as being obvious over the prior art, including Maloney. Specifically, Roxane contends that the Maloney reference teaches controlled-release oxymorphone formulations with 12-hour dosing intervals,

among other things. The *Kao* court, as detailed above, agreed, finding that Maloney rendered Endo's controlled-release oxymorphone composition obvious. *See In re Kao*, 639 F.3d at 1065-1066. Many of the issues that Endo is now attempting to relitigate have already been decided by the *Kao* court. For example, below is a comparison of claim 8 of the '859 application which the Federal Circuit held to be obvious and claim 40 of the '216 patent which Endo is asserting here (note that claim 40 depends from Claim 38 and thus incorporates by reference the limitations of claim 38):

'859 application claim 8 (held invalid in *Kao*)	**'216 patent claim 40 (depends from 38) (currently asserted)**
8. A method for treating pain in a human subject in need of acute or chronic pain relief, comprising the steps of: (a) Providing a solid oral dosage form comprising about 5 mg to about 80 mg oxymorphone or a pharmaceutically acceptable salt thereof in a controlled release delivery system with a release rate profile designed to provide an adequate blood plasma level over at least 12 hours to provide sustained pain relief over this same period, the system comprising a filler and a hydrophilic material, wherein oxymorphone is the sole active ingredient; and, (b) administering the dosage form to the subject, wherein the oxymorphone C_{max} is at least about 50% higher when the dosage form is administered to the subject under fed versus	38. A method for treating pain in a human subject in need of acute or chronic pain relief, comprising the steps of: (a) Providing a solid oral dosage form comprising about 5 mg to about 80 mg oxymorphone or a pharmaceutically acceptable salt thereof in a controlled release delivery system with a release rate profile designed to provide adequate blood plasma levels over at least 12 hours to provide sustained pain relief over this same period, **and wherein upon placement of the composition in an in vitro dissolution test comprising USP Paddle Method at 50 rpm in 500 ml media having a pH of 1.2 to 6.8 at 37° C., about 15% to about 50%, by weight, of the oxymorphone or salt thereof is released from the tablet at about 1 hour in the test, about 45% to about 80%, by weight, of the oxymorphone or salt thereof is released from the tablet at about 4 hours in the test, and at least about 80%, by weight, of the oxymorphone or salt thereof is released from the tablet at about 10 hours in the test; and** wherein oxymorphone is the sole active ingredient, (b) administering a single dose of the dosage form to the subject, wherein the oxymorphone C_{max} is at least 50% higher when the dosage form is administered to the subject under fed

fasted conditions.	versus fasted conditions. 40. The method of claim 38 **wherein the difference in the oxymorphone area under the curve $AUC_{(0\text{-inf})}$ between fed and fasted conditions is less than 20%.**

In holding claim 8 of the '859 application invalid, the *Kao* court held invalid solid oral dosage forms comprising about 5 mg to about 80 mg oxymorphone in a controlled release delivery system comprising a hydrophilic material with a release rate profile designed to provide sustained pain relief over at least 12 hours. Further, *Kao* held that the food effect limitation where the "oxymorphone C_{max} is at least about 50% higher when the dosage form is administered to the subject under fed versus fasted conditions" is an inherent property of oxymorphone that, as a matter of law, cannot change the obviousness determination. The only issues related to claim 40 that are not recited in claim 8 of the '859 application (as shown in red above), are (i) whether the dissolution profile of claim 40 is obvious over Maloney and (ii) whether the food effect limitation for $AUC_{(0\text{-inf})}$ is also inherent—where the food-effect for $AUC_{(0\text{-inf})}$ is calculated using the same food-effect study results (*i.e.*, oxymorphone blood levels) that are used to calculate the C_{max} food-effect that *Kao* already found inherent.

The *Kao* court addressed the issue of whether the Paddle Method dissolution profiles in Endo's patents were obvious over Maloney when it examined claims 1 and 20 of the '432 application. The dissolution profiles from claim 20 of the '432 application and claim 40 are provided below:

'432 application claim 20 (remanded in *Kao*)	**'216 patent claim 40 (depends from 38) (currently asserted)**
…wherein upon placement of the composition in an in vitro dissolution test comprising USP Paddle Method at 50 rpm in 500 ml media having a pH of 1.2 to 6.8 at 37° C., about 15%	…wherein upon placement of the composition in an in vitro dissolution test comprising USP Paddle Method at 50 rpm in 500 ml media having a pH of 1.2 to 6.8 at 37° C., about 15%

to about 50%, by weight, of the oxymorphone or salt thereof is released from the composition at about 1 hour in the test, about 45% to about 80%, by weight, of the oxymorphone or salt thereof is released from the composition at about 4 hours in the test, and at least about 80%, by weight, of the oxymorphone or salt thereof is released from the composition at about 10 hours in the test.	to about 50%, by weight, of the oxymorphone or salt thereof is released from the tablet at about 1 hour in the test, about 45% to about 80%, by weight, of the oxymorphone or salt thereof is released from the tablet at about 4 hours in the test, and at least about 80%, by weight, of the oxymorphone or salt thereof is released from the tablet at about 10 hours in the test…

The *Kao* court noted that there was insufficient evidence to support an obviousness finding between the Paddle Method dissolution profile claimed in the pending '432 application and the Basket Method dissolution profile described in Maloney, and the court remanded the case to the PTO on only that issue. Despite Endo's arguments to the contrary, the Federal Circuit found that all other claim limitations in claims 1 and 20 of the '432 application were either found in Maloney or were unpatentable because they were inherent to oxymorphone itself, leaving only the dissolution "gap" issue to be decided on remand.

On remand after *Kao*, the PTO concluded that it did not have the appropriate prior art in the record to establish a correlation between the two dissolution methods to support an obviousness finding. Roxane and the defendants in the present case, however, have that prior art and thus will be providing substantial evidence to bridge the dissolution gap at trial. Thus, the only remaining issue regarding validity of these patents for this Court to decide is whether the gap bridging evidence presented at trial is sufficient to render the claims obvious.

In addition, Endo argued at the Federal Circuit that the claim limitations regarding "food effects" and multiple drug plasma peaks were not inherent to oxymorphone. The *Kao* court disagreed and held that the claimed "food effects" and multiple peaks were in fact inherent to oxymorphone and not attributable to any specific formulation. *Id*. at 1068-1070. The *Kao* court further held that the inherent "food effects" add "nothing of patentable consequence." *Id*. at

1070. Endo never convinced the Federal Circuit or the Patent Office differently. Despite these findings against Endo, Endo persists in making the very same argument here.

Likewise, in an effort to rebut Roxane's showing of *prima facie* obviousness of the asserted claims of the patents-in-suit over Maloney and other references, Endo is *again* arguing that Maloney is not enabled for controlled-release oxymorphone formulations. The Federal Circuit already disposed of Endo's argument, stating that Endo's evidence "fall[s] short of establishing that the Maloney reference was non-enabling" for controlled-release oxymorphone formulations. *Id*. at 1071 In support of its holding, the *Kao* court noted that "obviousness does not require absolute predictability, only a reasonable expectation that the beneficial result will be achieved." *Id*. (citing *In re Merck & Co., Inc.,* 800 F.2d 1091, 1097 (Fed. Cir. 1986)).

Endo is making the exact same arguments in this case as it raised and lost previously in the PTO and at the Federal Circuit. The issues presented here are identical to those already litigated in *Kao*.

Moreover, the '432 and '859 applications and the '122 and '216 patents are all descended as continuations of a common ancestor, they each have the same patent specification, highly similar claim limitations, and almost identical subject matter. Therefore the Federal Circuit's findings in *In re Kao* regarding the '432 and 859 applications are directly applicable to the '122 and '216 patents.

Were the issues actually litigated and decided in the prior action? Yes. After exhausting numerous avenues with the PTO, Endo filed an appeal with the Federal Circuit. At each proceeding, Endo relied on its evidence regarding obviousness over Maloney, inherent properties of oxymorphone, and enablement of the Maloney reference, including at the oral

argument in the Federal Circuit.[2] On May 13, 2011, the court issued its opinion addressing these issues.

Did Endo have a full and fair opportunity to litigate the issues in the prior action? Yes. As noted above, Endo presented its arguments as to these issues to the fullest extent it desired at the PTO and at the Federal Circuit. Endo certainly had a full and fair opportunity (in fact, many full and fair opportunities) to litigate these issues. Simply because Endo disagrees with the Federal Circuit's findings does not permit Endo to make the same arguments it lost in a different venue.

Was resolution of the issue necessary for final judgment? Yes. The question the Federal Circuit addressed was whether the PTO was correct in rejecting the pending claims of the '432, '859, and '740 applications as obvious. To answer that question, the *Kao* court necessarily had to address and resolve the issues concerning the teachings of Maloney, whether Maloney was enabled, and whether certain claimed limitations are inherent properties of oxymorphone. In finding that Maloney was enabled for controlled-release oxymorphone formulations and that oxymorphone exhibits certain inherent properties upon absorption, the Federal Circuit was then able to determine that the case should be remanded for the issue concerning correlation of dissolution tests. There is no reason to burden the Court or the parties with having to relitigate the findings of the PTO and the Federal Circuit. *See*, *e.g.*, *Zdanok v. Glidden*, 327 F.2d 944, 955 (2d Cir. (1964) ("'Finality' [for the purposes of collateral estoppel] may mean little more than that the litigation of a particular issue has reached such a stage that a court sees no really good reason for permitting it to be litigated again.").

[2] *See* http://www.cafc.uscourts.gov/oral-argument-recordings/2010-1307/all.

III. CONCLUSION

For the reasons set forth above, Roxane respectfully requests that the Court preclude Endo from taking positions inconsistent with the Federal Circuit's findings in *In re Kao*, 639 F.3d 1057 (Fed. Cir. 2011).

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Respectfully Submitted,

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